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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/589,167	06/08/2000	Brendan Larder	07691.0006	9773

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EXAMINER

ZEMAN, MARY K

ART UNIT PAPER NUMBER

1631

DATE MAILED: 01/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/589,167

Applicant(s)

LARDER ET AL.

Examiner

Mary Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 8-12 and 23-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 13-22 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-7 and 13-22 in Paper No. 4 is acknowledged. The traversal is on the ground(s) that it would not pose a serious burden upon the office to search the four independent and distinct inventions as set forth in the Restriction Requirement. This is not found persuasive because each Invention sets forth differing methods, having differing ultimate goals, using differing method steps and data to obtain differing results. As such, each invention would require searching in non-overlapping search areas, and would require consideration of differing issues regarding enablement. As such, the search and examination of more than one Invention would pose an undue burden upon the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-13 and 23-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 4.

Information Disclosure Statement

The IDS, filed 9/7/00 has been entered and considered. An initialed copy of the form PTO-1449 is included with this action.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See, for example, page 14.

Claim Rejections - 35 USC § 112

Claims 1-7, 13-19, 20, 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 and 13-19 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the actual steps required to "predict resistance"

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that must be performed by the trained neural net. Without such steps explicitly recited, the “predicting” step is entirely unclear as to how such predicting is to be performed. Further, the method is lacking steps wherein a sample is obtained, and the genetic information of the pathogen is obtained from the sample. Without such steps, the method is not being performed on any real data, and is simply another training exercise using data already available in the database.

In claims 1, 13 and 20, it is unclear what exactly constitutes a trained neural network. Does it comprise the algorithms and the training data set? Or just the algorithms that result from modifications through training? How much training must occur? How much data, and what kind of data should be used in the training? For what is the network trained? The claim does not set forth that the network is trained for the particular method. It would appear that specific data and events, as well as specific algorithms and instructions, are required for such training. ? It would appear that, at the least, data regarding known mutations and resistance would be required to practice the method, but these things are not set forth. The limitations in claims 6, 7, 18 and 19 regarding the type of neural network do not address the training issue.

Further in claims 1, 13 and 20, the metes and bounds of the phrase “a determined genetic sequence” are unclear. Does Applicant intend the full DNA sequence of the entire genome of the pathogen? Or simply the presence or absence of particular sets of genes? Or the DNA sequences of certain genes? These types of data are not necessarily interchangeable.

In claims 21 and 22, the claims recite that the “disease is a pathogen” which is not strictly accurate. A disease is a collection of symptoms and pathologies which can be *caused by* a pathogen, but a disease is not the same as a pathogen.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1-5 and 13-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Comanor et al. (US 5,860,917).

The claims are drawn to methods of predicting whether a pathogen is resistant to a particular therapeutic agent using a trained neural network, and genetic data of the pathogen. No particular network structure is claimed, no particular training algorithm is specified, no particular data sets are required. The particular pathogens can include disease causing viruses such as HIV, HCV and HBV.

Comanor et al. (US 5,860,917) disclose methods of predicting whether a patient with a particular disease (infection with HIV, HCV, or HBV) will respond to a particular treatment or therapeutic agent (such as α -interferon). The statistical model generated by the methods of Comanor et al. appear to meet the limitations of a "trained neural network" in that a set of data is used which can be a genetic sequence of the pathogen (column 5 lines 59-60), and knowledge of sensitivity or resistance to a particular treatment or therapeutic agent. This data is used to train and develop a statistical model which is able to learn and predict resistance or sensitivity to a particular treatment (the SMILES analysis function). Comanor et al. note when using this function that "[o]bjects that are mathematically similar will have a high probability of having the same or very similar responses to treatment." (column 7 lines 23-26) Therefore, a patient sample containing a pathogen having the same or a highly similar genetic sequence as a sequence in the training set or database has a high probability of having the same response to the therapeutic agent. Comanor et al specifically contemplate viral inhibitors such as nucleoside analogs and protease inhibitors for HIV infection at column 12 lines 41-44. As such, this disclosure of Comanor et al. meet the limitations of the above rejected claims.

Claims 1-7 and 13-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Draghici et al. (April, 2000).

Claims 6, 7, and 18-19 add limitations to a feedforward neural network, and claims 20-22 are drawn to the neural network itself.

Draghici et al. (Draghici et al. *Correlation of HIV Protease Structure with Indinivir Resistance: a Data Mining and Neural Networks Approach*. Proceedings of SPIE, Volume 4057, April 2000, pages 319-329 in: Data Mining and Knowledge Discovery : Theory, Tools and

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Technology II.) disclose methods of predicting the resistance of a pathogen (HIV) to a therapeutic agent (Indinivir) using a feed forward neural network (p324). The genetic sequence of the protease gene of HIV-1 was used to model the protein structure, along with data regarding known mutations, and their associated resistance or sensitivity to Indinivir. The feed forward network comprised at least an input node, at least one hidden layer, and an output node. Therefore, the disclosure of Draghici et al. meets the limitations of the rejected claims.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Abidi et al. *Applying Knowledge Discovery to Predict Infectious Disease Epidemics* : PRICAI '98 : Topics in Artificial Intelligence. Springer-Verlag, Berlin, Germany, 1998, pages 170-181. Abidi et al. Disclose the use of feed forward neural networks in predicting resistance of various bacterial pathogens to antibiotics.

Almeida et al. *Application of Artificial Neural Networks to the Detection of Mycobacterium tuberculosis, its antibiotic resistance and prediction of Pathogenicity amongst Mycobacterium spp. Based on signature lipid biomarkers*. Binary Computing in Microbiology (1995) Vol. 7 No. 4-6, pages 159-166

Wu, C. (US 5,845,049 A1) discloses methods of using feed forward neural networks to find and predict particular motifs in protein sequences.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can generally be reached between the hours of 7:00 am and 1:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

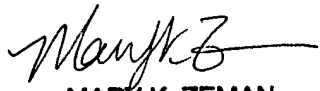
Official fax numbers for this Art Unit are: (703) 308-4242, (703) 872-9306. An *unofficial* fax number, direct to the Examiner is (703) 746 5279. Please call prior to use of this number.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the TC1600 Receptionist whose telephone number is (703) 308-0196.

mkz

1/23/02


MARY K. ZEMAN
PRIMARY EXAMINER
1/23/02